Current translational and clinical practices in hematopoietic cell and gene therapy.

Journal: Cytotherapy

Publication Year: 2012

Authors: David L Digiusto, Hans-Peter Kiem

PubMed link: 22799276

Funding Grants: Development of RNA-based approaches to stem cell gene therapy for HIV

Public Summary:
Clinical trials over the last 15 years have demonstrated that cell and gene therapy for cancer, monogenic and infectious disease is feasible and can lead to long-term benefit for patients. These trials however have been limited to proof of principle and were conducted on modest numbers of patients or over long periods of time. In order for these studies to move towards standard practice and commercialization, scalable technologies for the isolation, ex vivo manipulation and delivery of these cells to patients must be developed. Additionally, regulatory strategies and clinical protocols for the collection, creation and delivery of cell products must be generated. In this article we will review recent progress in hematopoietic cell and gene therapy, describe some of the current issues facing the field and discuss clinical, technical and regulatory approaches used to navigate the road to product development. The transition from the laboratory to the clinic (bench to bedside) is well charted for small molecules but less so for cellular therapeutics. Moving a cell product from the basic research laboratory, through process development and on to manufacturing and clinical trials is known as translational research and has become the focus of both federal and private investment. Passage through this proverbial "valley of death" is typically where most candidate therapeutics are stalled, many to never see the clinic. The funding of over 49 Clinical and Translational Science Award centers across the country reflects the National Institutes of Health (NIH) view that translational sciences are a high priority in the NIH roadmap for medical research. Like any new medical treatment, the initial years of clinical investigation defined both the utility and limitations of cellular therapy but also led to significant innovation and development of infrastructure in support of subsequent, more advanced studies. For example, bone marrow transplantation was one of the first and still most widely used forms of cell therapy and has helped define both the therapeutic potential of and significant hurdles in developing stem cell products. An important development in cellular therapy was the discovery of a subpopulation of white blood cells expressing the CD34 antigen that contains virtually all of the long-term hematopoietic reconstituting (stem cell) activity in a bone marrow graft. The correlation between the number of CD34+ cells transplanted and successful engraftment has helped establish the first stem cell therapy dosing specification to be used in standard clinical practice. Moreover, CD34+ cells have become the substrate of choice for genetic modification to treat a number of disease indications with an autologous product. In a similar fashion, allogeneic transplantation of bone marrow has led to an understanding of the benefits transfer of T-cells with anti-tumor as well as the potentially devastating consequences of T-cell mediated graft versus host disease (GVHD). These latter observations have played a major role in the development of adoptive immunotherapy (AI) strategies for cancer and infectious disease and will be used as examples of how subsequent cell therapies may be developed.

Scientific Abstract:
Clinical trials over the last 15 years have demonstrated that cell and gene therapies for cancer, monogenic and infectious disease are feasible and can lead to long-term benefit for patients. However, these trials have been limited to proof-of-principle and were conducted on modest numbers of patients or over long periods of time. In order for these studies to move towards standard practice and commercialization, scalable technologies for the isolation, ex vivo manipulation and delivery of these cells to patients must be developed. Additionally, regulatory strategies and clinical protocols for the collection, creation and delivery of cell products must be generated. In this article we review recent progress in hematopoietic cell and gene therapy, describe some of the current issues facing the field and discuss clinical, technical and regulatory approaches used to navigate the road to product development.